Mechanisms of Reproductive Toxicity

AILEEN F. KEATING and PATRICIA B. HOYER

1 INTRODUCTION

Today, women are entering the workplace in record numbers. Many are postponing childbearing to establish a career. For this reason and because people are exposed to ever-increasing concentrations of environmental chemicals, there is an increased awareness of the impact of environmental chemicals on reproductive health. The female must perform two distinct reproductive functions: development and support of female germ cells and maintenance of the fetus until it can survive in the outside world. The reproductive functions of the male include production of the male germ cell (spermatogenesis) and male steroid hormones (steroidogenesis). Therefore, reproductive toxicology involves detecting and understanding potentially detrimental environmental influences on reproductive success in females and males.

This field has been developing in response to observations linking clustered effects in humans to specific types of exposures. There have been several examples of how xenobiotics in the form of pharmaceuticals can impact reproductive function in humans. One is the effect of the sedative thalidomide, prescribed to women in the 1950s for morning sickness during early pregnancy (Seegmiller, 1997). A greatly increased incidence of children born with developmental organ and limb malformations was traced to *in utero* exposure to thalidomide. This drug was reported to have been responsible for 8000 malformed children over a two-year period. Whereas thalidomide is an example involving developmental limb defects, reproductive effects in humans have been seen with the synthetic estrogen, diethylstilbestrol (DES). From the 1940s to 1960s, DES was widely prescribed for women with high-risk pregnancies. In 1971, Herbst, Ulfelder and Poskanzer (1971) observed an increased incidence of rare vaginal clear cell adenocarcinoma in their daughters who had been exposed *in utero* to DES. Subsequent research has demonstrated that prenatal exposure to DES can also cause fertility defects, teratogenesis, and neoplasia throughout the male and female reproductive tracts (Hendry *et al.*, 1999).

The following chapter will outline what is currently known about how xenobiotics can impact reproductive function in females and males. The information is based

Pharmaceutical Sciences Encyclopedia: Drug Discovery, Development, and Manufacturing
Edited by Shayne C. Gad